Review Article

A Review on Pathogenesis and Epidemiology of Coronavirus Disease (Covid-19)

Mohammed Misbah Ul Haq

Department of Pharmacy Practice, Deccan School of Pharmacy, Darussalam, Nampally, Hyderabad, Telangana, INDIA.

ABSTRACT

Coronavirus disease (COVID-19) is a communicable disease and SARS-COV 2 is the causative agent of a potentially fatal disease this is of exceptional international public fitness concern. Based on the large number of infected people that were exposed to the most animal market in Wuhan City, China, its miles cautioned that this is in all likelihood the zoonotic foundation of COVID-19. Person-to-individual transmission of COVID-19 infection led to the isolation of sufferers that were eventually administered plenty of treatments. Extensive measures to lessen the individual-to-character transmission of COVID-19 were implemented to govern the current outbreak. Special interest and efforts to guard or reduce transmission have to be implemented in susceptible populations which include children, health care providers and elderly people. In this review, the Pathophysiology and Epidemiology of COVID-19 are highlighted.

Key words: COVID-19, Pathophysiology, Epidemiology, Coronavirus disease 2019, SARS-COV 2.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), a communicable disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). First identified in December 2019 in Wuhan, Hubei province (China) and has spread globally, leading to an ongoing pandemic.[1] Recently, about 3.66 million cases were reported over 187 countries and territories, resulting in over 0.28 million deaths. Over 1.19 million people recovered. Common symptoms like fever, cough, fatigue, shortness of breath and loss of smell and taste.[2] While many of cases lead to mild symptoms, some may attain viral infection, multi-organ failure, or cytokine storm.[3-6] The time from exposure to onset of manifestations is usually around 5 days but may range from 2 to 14 days (Figure 1).[7]

The virus primarily advances between individuals during close contact, [a] often through small droplets produced by coughing, [b] sneezing and talking. The droplets usually fall to the ground or onto the surfaces rather than enduring in the air over prolonged interval.[8] Individuals can also become infected by touching a contaminated surface then touching their face.[9] On surfaces, the number of virus declines over time until it's insufficient to stay infectious, but it should be detected for hours or days.[9] It's most contagious during the primary 3 days after the onset of symptoms, although spread could also be possible before symptoms appear and in later stages of the disease.

The Standard procedure of diagnosis is by real-time reverse transcription-polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab or throat swab. Chest CT imaging can also be helpful for diagnosis in individuals where there's a high suspicion of infection supported symptoms and risk factors; although, guidelines don't suggest using it for routine screening (Figure 2).[9]

Recommended measures to forestall infection include frequent hand washing, maintaining physical distance from others (especially from those with symptoms), quarantine, covering coughs and keeping unwashed hands off from the face.[10]

Additionally, make use of a face covering is usually recommended for those that

DOI: 10.5530/ijopp.13.4.50

Address for correspondence:
Dr. Mohammed Misbah Ul Haq
Deccan School of Pharmacy, Darussalam, Hyderabad-500001, Telangana, INDIA.
Phone no: +91 7673930461
Email Id: misbahjed@gmail.com

www.ijopp.org

suspect they possess the virus and their caregivers. Recommendations for face-covering use by the common public vary; requiring their use.[11] There's limited proof for or against the utilization of masks (medical or other) in healthy individuals within the wider community. According to the World Health Organization, there aren't any available vaccines nor specific antiviral treatments for COVID-19. On 1 May 2020, the U.S. gave Authorization to the Antiviral Drug 'Remdesivir' for individuals hospitalized with severe COVID-19. Management involves the treatment of symptoms, supportive care, isolation and experimental steps. The World Health Organization (WHO) announced the COVID-19 outbreak a Public Health Emergency of International Concern (PHEIC) on 30 January 2020 and a pandemic on 11 March 2020. Local transmission of the infection has spread in most countries across all six regions of WHO.

PATHOGENESIS

Lungs are affected by COVID 19 because the virus accesses host cells via the enzyme angiotensin-converting enzyme 2 (ACE2), which is most ample in type II alveolar cells of the lungs (Figure 3).[12] The virus uses a special surface glycoprotein a spike (peplomer) to attach to ACE2 and enter the host cell.[13] The density of ACE2 in each tissue correlates with the severity of the disease in that tissue and some have suggested that decreasing ACE2 activity might be protective.[14,15]

Another prospect is that increasing ACE2 using Angiotensin II receptor blocker medications can be protective and these hypotheses to be tested. As the alveolar disease develops, respiratory failure may occur and death may follow.[15]

SARS-CoV-2 may additionally cause respiratory failure by affecting the brainstem as other coronaviruses have found to invade the central nervous system (CNS). Whilst, the virus has been detected in cerebrospinal fluid of post-mortem, the precise mechanism by which it permeates the CNS remains unclear and involve invasion of peripheral nerves shown the low levels of ACE2 in the brain.[16,17]

The virus affects GI organs as ACE2 is amply expressed in the glandular cells of the gastric; duodenal and rectal epithelium,[18] endothelial cells and enterocytes of the small intestine.[19]

The virus can cause acute myocardial injury and chronic damage to the circulatory system.[20] An acute cardiac injury was found in 12% of infected people admitted to the hospital in Wuhan, China,[21] and is more frequent in severe disease (Figure 4).[22]

Rates of cardiovascular symptoms are high, owing to the systemic inflammatory response and immune system disorders throughout the disease development, but

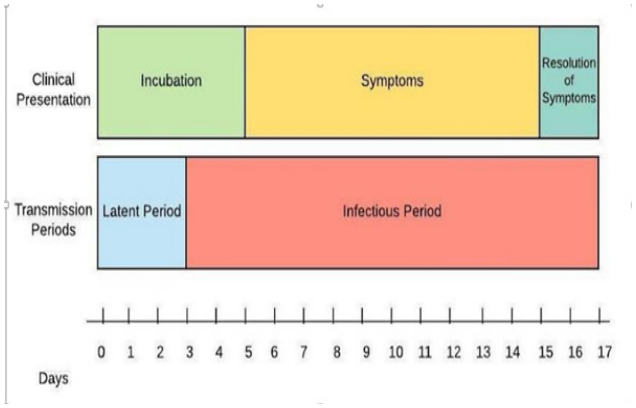

Figure 1: Representation of COVID-19 Clinical and Transmission Periods.[23]

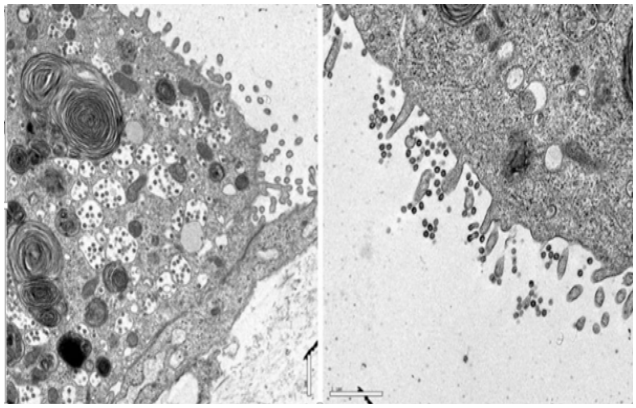

Figure 2: Typical CT imaging findings and CT imaging of rapid progression stage.[24]

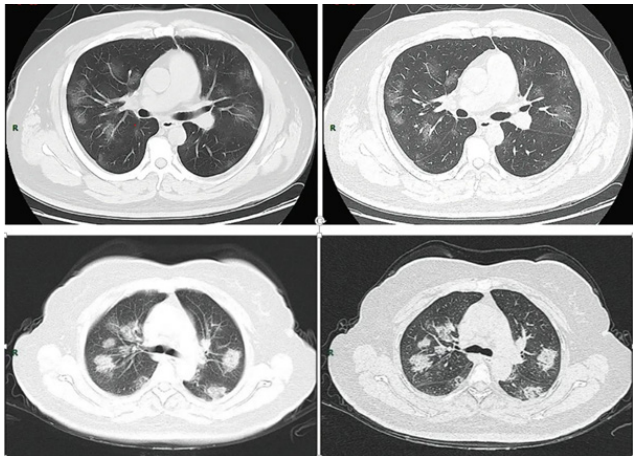

Figure 3: Human alveolar type II cells infected with SARS-CoV. Human type II cells were isolated, cultured *in vitro* and then infected with SARS-CoV. Viral particles are seen in double membrane vesicles in the type II cell.24

acute myocardial injuries can also be linked to ACE2 receptors in the heart.[20] ACE2 receptors are excessively shown in the heart and are involved in heart function.[20,26] A high incidence of thrombosis (31%) and venous thromboembolism (25%) have been found in ICU patients with COVID 19 infections and may be related to poor prognosis.[27]

Blood vessel dysfunction and clot formation (as suggested by high D-dimer levels) are thought to play a significant role in mortality, incidences of clots leading to pulmonary embolisms and ischemic events within the brain have been noted as complications resulting in death in patients infected with SARS-CoV-2.

Infection appears to produce a sequence of vasoconstrictive responses in the body, constriction of blood vessels within the circulation has been posited as a mechanism during which oxygenation decreases alongside the presentation of viral pneumonia.

Another common cause of death are problems related to the kidneys —SARS-CoV-2 directly infects kidney cells, as confirmed in post-mortem studies.

Acute kidney injury is a common complication and reason for death; this is often more significant in patients with already compromised kidney function, especially in people with pre-existing chronic conditions such as hypertension and diabetes which specifically cause nephropathy eventually.

Autopsies of individuals who died of COVID 19 have found diffuse alveolar damage (DAD) and lymphocyte suppressing inflammatory infiltrates within the lung.[28]

Based on the cells that are probably infected, COVID-19 can be divided into 3 phases that are identical to different stages of the disease.

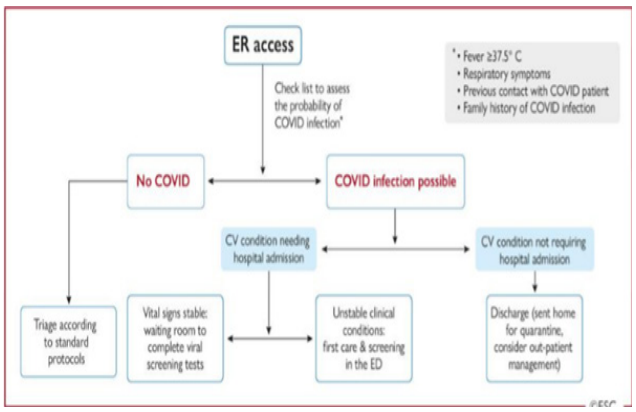

Figure 4: Algorithm for triaging patients admitted to the ER for a suspected.[25]

Stage 1: Asymptomatic state (initial 1–2 days of infection)

Stage 2: Upper airway and conducting airway response (next few days)

Stage 3: Hypoxia, ground glass infiltrates and progression to Respiratory Distress Syndrome (ARDS)

IMMUNOPATHOLOGY

Although SARS-COV-2 contains a tropism for ACE2-expressing epithelial cells of the respiratory tract, patients with severe COVID 19 have symptoms of systemic hyper inflammation. Laboratory findings of elevated IL-2, IL-7, IL-6, granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon-γ inducible protein 10 (IP-10), monocyte chemo attractant protein 1 (MCP-1), macrophage inflammatory protein 1-α (MIP-1α) and tumor necrosis factor-α (TNF-α) indicative of cytokine release syndrome (CRS) suggest an underlying immunopathology.[23]

Additionally, individuals with COVID 19 and acute respiratory distress syndrome (ARDS) have classical serum biomarkers of CRS, including elevated C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer and ferritin.[29]

Systemic inflammation leading to vasodilation, allowing inflammatory lymphocytic and monocytic infiltration of the lung and the heart. Particular, pathogenic GM-CSF-secreting T-cells were shown to correspond with the improvement of inflammatory IL-6-secreting monocytes and severe lung pathology in COVID 19 convalescents. Lymphocytic infiltrates have been reported at autopsy.[28]

EPIDEMIOLOGY

Several steps are commonly used to quantify mortality. These numbers vary by region and over time and are impacted by the volume of testing, healthcare system standard, treatment options, time since the inceptive outbreak and public attributes such as age, gender and overall health. The death-to-case ratio reflects the no. of deaths divided by the no. of diagnosed cases in a specified time interim. Based on Johns Hopkins University statistics, the global death-to-case ratio is 7.0% (2,57,301/36,63,911) as of 6 May 2020. The number varies by region (Figure 5-9).[30]

Other steps include the case fatality rate (CFR), which contemplates the percent of diagnosed people who die from a disease and the infection fatality rate (IFR), which contemplates the percent of infected people (diagnosed

and undiagnosed) who die from a disease.

These statistics are not time-bound and follow a particular population from infection by case resolution. Many scholars have attempted to seek out the numbers for specific populations.

Outbreaks have come about in prisons due to jam-packed and an inability to implement requisite social distancing.[31]

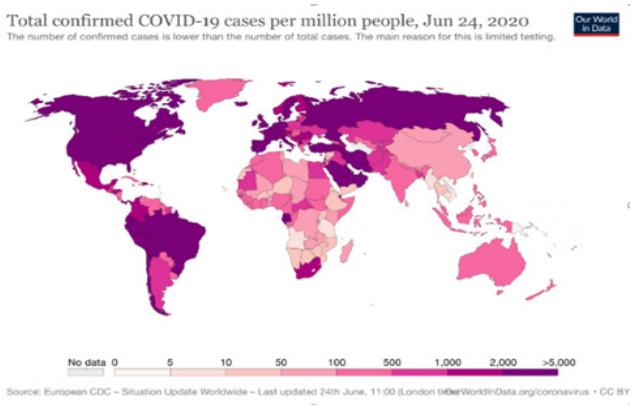

Figure 5: Total confirmed cases over time and Total deaths over time.

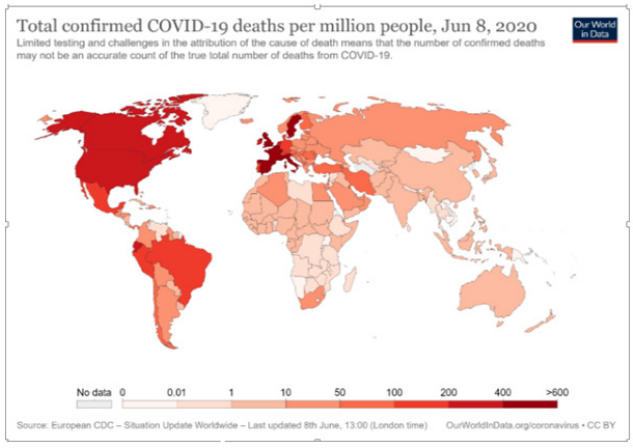

Figure 6: Total confirmed case and Total confirmed deaths due to COVID-19 per million people.

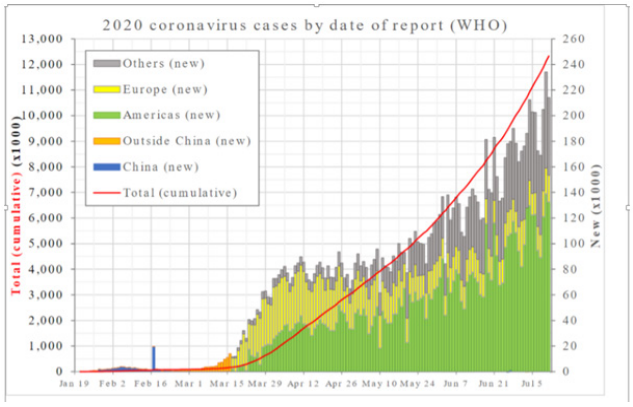

Figure 7: Epidemic curve of COVID-19.[32]

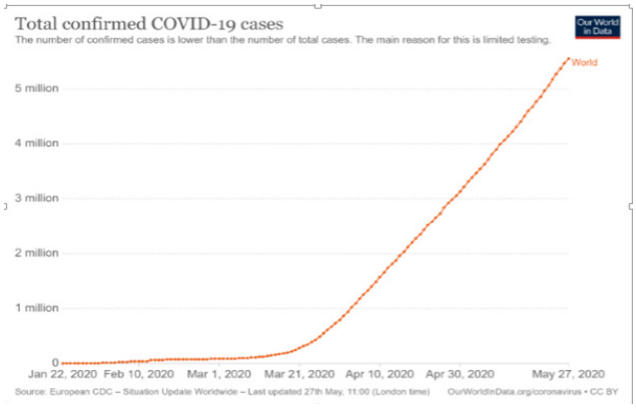

Figure 8: Total confirmed cases over time

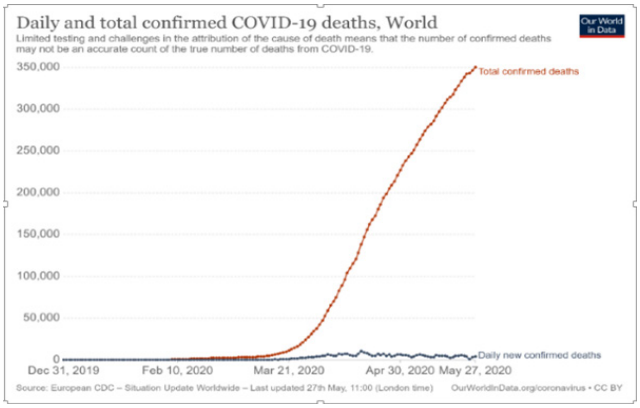

Figure 9: Total deaths over time.

In the United States, the prisoner population is aging and many of them are at high risk for poor outcomes from COVID-19 due to high rates of pre-existing heart and lung disease, poor access to high-class healthcare.[31]

INFECTION FATALITY RATE (IFR)

Our World in Data, as of March 25, 2020, the infection fatality rate (IFR) cannot be accurately calculated. In February, the World Health Organization estimated the IFR at 0.94%, with a confidence interval between 0.37% to 2.9%.

The University of Oxford Centre for Evidence-Based Medicine (CEBM) estimated a worldwide CFR of 0.72 % and IFR of 0.1% to 0.36%. According to CEBM, random antibody testing in Germany suggested an IFR of 0.37% (0.12% to 0.87%) there, but there have been concerns about false positives.[33]

Firm lower limits of infection fatality rates have been established in a no. of locations. In NYC, with a population of 8.4 million, as of May 7, 14,162 (0.17% of the population) died from COVID-19. In Bergamo province, where 0.57% of the population died. To get

a clear view of the no. of individuals infected by initial antibody testing, yet no valid scientific reports are based on any of them.

GENDER DIFFERENCES

The influence of the pandemic and its mortality rate are unrelated for men and women. Mortality is higher in men in studies overseen in China and Italy.[34-36] The higher risk for men seems in their 50s and set out to taper off at 90. In China, the death rate was 2.8 % for men and 1.7 % for women. The exact reasons for this gender-difference are not well known, but genetic and behavioral factors could be a reason.

Gender-based immunological differences, a lower prevalence of smoking in women and men evolving co-morbid states such as hypertension at a younger age than women could have put up to the higher mortality in men. In Europe, of those infected with COVID-19, 57% were men; of those infected with COVID-19 died, 72% were men.[37]

As of April 2020, the U.S. government is not following gender-related details of COVID-19 infections. Research has shown that viral ailments like Ebola, HIV, influenza and SARS affect men and women differently.[37]

A higher proportion of healthcare assistant, particularly nurses, are women and have a higher possibility of being exposed to the virus.[38] School closures, lockdowns and reduced ingress to healthcare following the 2019–20 coronavirus pandemic may differentially affect the genders and possibly overstress existing gender disparity.[38]

ETHNIC VARIANCES

In the U.S., a greater proportion of deaths due to COVID-19 have occurred among African Americans.[39] Systemic factors that prevent African Americans from carrying out social distancing comprise their gathering in crowded inadequate housing and key jobs such as public transit employees and health-care workers.

Greater prevalence of lacking health assurance and care and of primary conditions such as diabetes, hypertension and heart disease also increase their risk of death.[40] Similar matters affect Native American and Latino communities.[39] Leaders called for efforts to research and address the disparities.[41]

PRE-EXISTING RESPIRATORY PROBLEMS

Individuals with pre-existing respiratory problems is infected with COVID-19, are at greater risk for severe symptoms. COVID-19 also poses a greater risk to people who misuse methamphetamines and opioids, as their drug use may have caused lung damage.

CONCLUSION

This review shows a holistic picture of the current study in response to the outbreak of COVID-19. During this early period, many studies have been published exploring the epidemiology, causes, signs and symptoms and diagnosis and prevention and control of the coronavirus disease.

Most studies cornerstone on the epidemiology and potential causes.

However, studies investigating prevention and control steps have begun to constantly increase. The COVID-19 pandemic is spreading rapidly, the case rates and CFRs continue to change instantly. Identifying clinical characteristics, developing and identifying relevant diagnostic criteria and providing efficacious treatment and management is crucial for overcoming the pandemic.

ACKNOWLEDGEMENT

I sincerely thank "Almighty Allah" for his grace for the successful and timely completion of my work.

CONFLICT OF INTEREST

The author declares that there are no conflicts of interest.

ABBREVIATIONS

COVID-19: Coronavirus Disease 2019; **SARS-COV 2:** Severe acute respiratory syndrome Coronavirus 2; **rRT-PCR:** real-time reverse transcription-polymerase chain reaction; **CT:** Computed tomography; **U.S:** United States; **WHO:** World Health Organization; **PHEIC:** Public Health Emergency of International Concern; **ACE2:** Angiotensin-Converting Enzyme 2; **CNS:** Central Nervous System; **GI:** Gastrointestinal; **ER:** Emergency Room; **ICU:** Intensive Care Unit; **DAD:** Diffuse Alveolar Damage; **ARDS:** Acute Respiratory Distress Syndrome; **IL:** Interleukins; **GM-CSF:** Granulocyte-Macrophage Colony-Stimulating Factor; **IP:** Inducible Protein; **MCP:** Monocyte Chemoattractant Protein; **MIP:** Macrophage Inflammatory Protein; **TNF:** Tumor Necrosis Factor; **CRS:** Cytokine Release Syndrome; **CRP:** C-reactive protein; **LDH:** Lactate Dehydrogenase; **CFR:** Case Fatality Rate; **IFR:** Infection Fatality Rate; **CEBM:** Centre for Evidence-Based Medicine; **NYC:** New York City; **HIV:** Human Immunodeficiency Virus; **SARS:** Severe Acute Respiratory Syndrome.

REFERENCES

1. Hui DS, Azhar EI, Madani TA, Ntoumi F, Kock R, Dar O. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health: The latest 2019 novel coronavirus outbreak in Wuhan, China, International Journal of Infectious Diseases. 2020;91:264-6.
2. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, *et al*. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. Plos One. 2020;15(6):e0234765
3. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the ‹Cytokine Storm› in COVID-19. J Infect. 2020;80(6):607-13.
4. Murthy S, Gomersall CD, Fowler RA. Care for Critically Ill Patients with COVID-19. JAMA. 2020;323(15):1499.
5. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, DiNapoli R. Features, Evaluation and Treatment Coronavirus (COVID-19), Stat Pearls. Treasure Island (FL): Stat Pearls Publishing.
6. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, *et al.* COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy and Follow-up. Journal of the American College of Cardiology. 2020;75(23):2950-73.
7. Velavan TP, Meyer CG. The COVID-19 epidemic, Tropical Medicine and International Health. 2020;25(3):278-80.
8. Stadnytskyi V, Bax CE, Bax A, Anfinrud P. The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission. Proceedings of the National Academy of Sciences of the United States of America. 2020;117(22):11875-7.
9. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients. American Journal of Roentgenology. 2020;215(1):87-93.
10. Nussbaumer-Streit B, Mayr V, Dobrescu AI, Chapman A, Persad E, Klerings I. Quarantine alone or in combination with other public health measures to control COVID-19: A rapid review. The Cochrane Database of Systematic Reviews. 2020;4:CD013574.
11. Feng S, Shen C, Xia N, Song W, Fan M, Cowling BJ. Rational use of face masks in the COVID-19 pandemic. The Lancet, Respiratory Medicine. 2020;8(5):434-6.
12. Verdecchia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. European Journal of Internal Medicine. 2020;76:14-20.
13. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nature Microbiology. 2020;5(4):562-9.
14. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: Molecular mechanisms and potential therapeutic target. Intensive Care Medicine. 2020;46(4):586-90.
15. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, *et al*. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. International Journal of Oral Science. 2020;12(1):8.
16. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. Journal of Medical Virology. 2020;92(6):552-5.
17. Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction and Proposed Neurotropic Mechanisms. ACS Chemical Neuroscience. 2020;11(7):995-8.
18. Gu J, Han B, Wang J. COVID-19: Gastrointestinal Manifestations and Potential Fecal-Oral Transmission. Gastroenterology. 2020;158(6):1518-9.
19. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, Goor HV. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus: A first step in understanding SARS pathogenesis. The Journal of Pathology. 2020;203(2):631-7.
20. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nature Reviews, Cardiology. 2020;17(5):259-60.
21. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
22. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.
23. Mason RJ. Pathogenesis of COVID-19 from a cell biology perspective. The European Respiratory Journal. 2020;55(4):2000607.
24. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: A multicenter study. Am J Roentgenol. 2020;214(5):1-6.
25. Han Y, Zeng H, Jiang H, Yang Y, Yuan Z, Cheng X, *et al*. CSC Expert Consensus on Principles of Clinical Management of Patients with Severe Emergent Cardiovascular Diseases during the COVID-19 Epidemic. Circulation. 2020;141(20):e810-6.
26. Turner AJ, Hiscox JA, Hooper NM. ACE2: From vasopeptidase to SARS virus receptor. Trends in Pharmacological Sciences. 2020;25(6):291-4.
27. Klok FA, Kruip MJ, DerMeer NJV, Arbous MS, Gommers DA, Kant KM, *et al*. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thrombosis Research. 2020;191:145-7.
28. Barton LM, Duval EJ, Stroberg E, Ghosh S, Mukhopadhyay S. COVID-19 Autopsies, Oklahoma, USA. American Journal of Clinical Pathology. 2020;153(6):725-33.
29. Zhang C, Wu Z, Li JW, Zhao H, Wang GQ. The cytokine release syndrome (CRS) of severe COVID-19 and Interleukin-6 receptor (IL-6R) antagonist Tocilizumab may be the key to reduce the mortality. International Journal of Antimicrobial Agents. 2020;55(5):105954.
30. Lazzerini M, Putoto G. COVID-19 in Italy: Momentous decisions and many uncertainties. The Lancet, Global Health. 2020;8(5):e641-2.
31. Hawks L, Woolhandler S, McCormick D. COVID-19 in Prisons and Jails in the United States. JAMA Internal Medicine. 2020;1856.
32. Siordia J. Epidemiology and Clinical Features of COVID-19: A Review of Current Literature. Journal of Clinical Virology. 2020;127:104357.
33. Wilson L. SARS-CoV-2, COVID-19, Infection Fatality Rate (IFR) Implied by the Serology, Antibody, Testing in New York City, SSRN. 2020;3590771.
34. Wenham C, Smith J, Morgan R, COVID-19: The gendered impacts of the outbreak. Lancet. 2020;395(10227):846-8.
35. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China:A descriptive study. Lancet. 2020;395(10223):507-13.
36. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. Clinical Immunology. 2020;215:108427.
37. Hu Y, Sun J, Dai Z, Deng H, Li X, Huang Q, *et al.* Prevalence and severity of corona virus disease 2019 (COVID-19): A systematic review and meta-analysis. Journal of Clinical Virology. 2020;127:104371.
38. Leiwen F, Wang B, Yuan T, Chen X, Ao YF, Thomas L, *et al.* Huachun, Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. Journal of Infection. 2020;80(6):656-65.
39. Dorn AV, Cooney RE, Sabin ML. COVID-19 exacerbating inequalities in the US. Lancet. 2020;395(10232):1243-4.
40. Adams ML, Katz DL, Grandpre J. Population-Based Estimates of Chronic Conditions Affecting Risk for Complications from Coronavirus Disease, United States. Emerging Infectious Diseases. 2020;26(8):1831.
41. Laurencin CT, McClinton A. The COVID-19 Pandemic: A Call to Action to Identify and Address Racial and Ethnic Disparities. Journal of Racial and Ethnic Health Disparities. 2020;7(3):398-402.